

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

What is claimed is:

1. (withdrawn) A method comprising:

providing a fluid flow path, the fluid flow path having first and second ends, a fluid flow controller effective to variably impose a positive or negative pressure on the flow path to cause controlled fluid flow through the fluid flow path in a first or second direction at predetermined rates, and a capture zone between the first and second ends, wherein a fixed magnetic field intercepts the fluid flow path in the capture zone;

providing in the fluid flow path a first mixture including a plurality of solid magnetic particles dispersed in a carrier medium;

passing the first mixture through the capture zone at a first predetermined capture rate whereby a major portion of the magnetic particles become trapped in the capture zone by the force of the magnetic field and thereby separated from the carrier medium to form a first magnetic particle isolate;

perfusing the first magnetic particle isolate with a first dispersion medium;
and

pulsing the first dispersion medium through the capture zone at a first predetermined dispersion rate effective to dislodge the first magnetic particle isolate from the capture zone, move the magnetic particles from the magnetic field, and suspend the magnetic particles in the first dispersion medium to provide a second mixture.

2. (withdrawn) The method in accordance with claim 1 wherein the fixed magnetic field has a strength that is substantially constant during said passing of the first mixture, said perfusing, said pulsing and said passing of the second mixture.

3. (withdrawn) The method in accordance with claim 1 wherein the fixed magnetic field is provided by a permanent magnet having a fixed relationship to the fluid flow path.

4. (withdrawn) The method in accordance with claim 1 wherein the fixed magnetic field is provided by an electromagnet that has a fixed relationship to the fluid flow path and a that produced a fixed magnetic field.

5. (withdrawn) The method in accordance with claim 1 wherein the magnetic particles include a surface-bound selective agent featuring selective affinity for a target substance.

6. (withdrawn) The method in accordance with claim 5 wherein the magnetic particles with surface-bound selective agents are effective to selectively retain a chemical or biological species in a sample.

7. (withdrawn) The method in accordance with claim 1 wherein the magnetic particles include properties suitable for adsorption of multiple target substances via a non-specific interaction.

8. (withdrawn) The method in accordance with claim 7 wherein the non-specific interaction is selected from the group consisting of an electrostatic interaction, a van der Waals interaction, dipole-dipole interaction and a hydrogen bonding interaction.

9. (withdrawn) The method in accordance with claim 6 wherein the first dispersion medium includes the sample.

10. (withdrawn) The method in accordance with claim 6 wherein the selective agent is effective to retain a biological species in a sample, and wherein the selective

agent is selected from the group consisting of an antigen, an antibody, a protein receptor, a ligand, an oligonucleotide, streptavidin, avidin, biotin and lectin.

11. (withdrawn) The method in accordance with claim 10 wherein the selective agent is an antibody.

12. (withdrawn) The method in accordance with claim 6, wherein the sample includes an analyte sample for an ELISA assay; wherein the selective agent is an antibody that selectively retains the analyte; and wherein the sample further includes an analyte-enzyme conjugate.

13. (withdrawn) The method in accordance with claim 12, wherein the analyte-enzyme conjugate comprises an enzyme having a specific catalytic activity and specificity for an analysis reagent.

14. (withdrawn) The method in accordance with claim 6 wherein the carrier medium includes the sample.

15. (withdrawn) The method in accordance with claim 14 wherein the mixture is incubated for a first period of time effective to cause the selective agent to contact and retain the species.

16. (withdrawn) The method in accordance with claim 15 wherein the first dispersion medium is a first wash solution.

17. (withdrawn) The method in accordance with claim 16, further comprising passing the second mixture through the capture zone at a second predetermined capture rate at which rate a major portion of the magnetic particles become trapped in the capture zone by the force of the magnetic field and thereby removed from the first dispersion medium to form a second magnetic particle isolate.

18. (withdrawn) The method in accordance with claim 17, further comprising:
perfusing the second magnetic particle isolate with a second dispersion medium; and
pulsing the second dispersion medium through the capture zone at a second predetermined dispersion rate effective to dislodge the second magnetic particle isolate from the capture zone, move the magnetic particles from the magnetic field, and suspend the magnetic particles in the second dispersion medium to provide a third mixture.
19. (withdrawn) The method in accordance with claim 18 wherein the second dispersion medium comprises an analysis reagent.
20. (withdrawn) The method in accordance with claim 19, further comprising passing the third mixture through the capture zone at a third predetermined capture rate at which rate a major portion of the magnetic particles become trapped in the capture zone by the force of the magnetic field and thereby removed from the second dispersion medium to form a third magnetic particle isolate.
21. (withdrawn) The method in accordance with claim 20 wherein the flow path further includes a detection zone, and wherein a detector is positioned to detect a physical or chemical property of a fluid in the detection zone; and further comprising, after passing the third mixture through the capture zone, detecting a physical or chemical property of a member selected from the group consisting of the second dispersion medium and the third magnetic particle isolate.
22. (withdrawn) The method in accordance with claim 21 wherein the analysis reagent is a coloring agent; and wherein the detector is an optical detector.

23. (withdrawn) The method in accordance with claim 22, further comprising: passing the second solution through the detection zone; and measuring the property of the second solution.

24. (withdrawn) The method in accordance with claim 18 wherein the second dispersion medium comprises a second wash solution.

25. (withdrawn) The method in accordance with claim 24, further comprising passing the third mixture through the capture zone at a third predetermined capture rate at which rate a major portion of the magnetic particles become trapped in the capture zone by the force of the magnetic field and thereby removed from the second dispersion medium to form a third magnetic particle isolate.

26. (withdrawn) The method in accordance with claim 25, further comprising:

perfusing the third magnetic particle isolate with a third dispersion medium; and

pulsing the third dispersion medium through the capture zone at a third predetermined dispersion rate effective to dislodge the third magnetic particle isolate from the capture zone, move the magnetic particles from the magnetic field, and suspend the magnetic particles in the third dispersion medium to provide a fourth mixture.

27. (withdrawn) The method in accordance with claim 26, further comprising passing the fourth mixture through the capture zone at a fourth predetermined capture rate at which rate a major portion of the magnetic particles become trapped in the capture zone by the force of the magnetic field and thereby removed from the third dispersion medium to form a fourth magnetic particle isolate.

28. (withdrawn) The method in accordance with claim 27 wherein the flow path further includes a detection zone, and wherein a detector is positioned to detect a physical or chemical property of a fluid in the detection zone; and further comprising, after passing the fourth mixture through the capture zone, detecting a physical or chemical property of a member selected from the group consisting of the third dispersion medium and the fourth magnetic particle isolate.

29. (withdrawn) The method in accordance with claim 28 wherein the second dispersion medium comprises an analysis reagent.

30. (withdrawn) The method in accordance with claim 29 wherein the analysis reagent is a coloring agent; and wherein the detector is an optical detector.

31. (withdrawn) The method in accordance with claim 1 wherein the magnetic field has a field gradient in the capture zone of from about 0.1 to about 2 kGauss/cm.

32. (withdrawn) The method in accordance with claim 1 wherein the flow path has a volume of from about .01 to about 50 μ L.

33. (withdrawn) The method in accordance with claim 1 wherein the flow path has an average diameter of from about 0.001 to about 5 mm.

34. (withdrawn) The method in accordance with claim 1 wherein the first predetermined capture rate is from about 1.0 to about 13mm/s.

35. (withdrawn) The method in accordance with claim 1 wherein the first predetermined dispersion rate is from about 250 to about 2500 mm/s.

36. (withdrawn) The method in accordance with claim 1 wherein the flow path is a microchannel.

37. (withdrawn) The method in accordance with claim 1 wherein said passing of the first mixture comprises passing in a first direction; wherein said passing of the first dispersion medium comprises passing in a second direction opposite the first direction; and wherein said passing of the second mixture comprises passing in the first direction.

38. (withdrawn) The method in accordance with claim 1 wherein the flow controller comprises:

a multiport selection valve including a primary port and a plurality of secondary ports, wherein a first secondary port is fluidly connected to the inlet of the fluid flow path;

a holding coil having a proximal end and a distal end; wherein the distal end is fluidly connected to the primary port of the selection valve;

a three-way valve having a first port fluidly connected to the proximal end of the holding coil; a second port fluidly connected to a variable speed reversible pump; and a third port fluidly connected to a source of a wash composition.

39. (withdrawn) The method in accordance with claim 38 wherein the variable speed reversible pump is a stepper-motor-driven syringe pump.

40. (withdrawn) The method in accordance with claim 38 wherein the multiport selection valve, the three-way valve and the pump are controlled by a pre-programmed computer.

41. (withdrawn) The method in accordance with claim 1, wherein the flow path in the capture zone is substantially free from fixed magnetizable solid matrix structures.

42. (Currently amended) An apparatus, comprising:
a fluid flow path, the fluid flow path having first and second ends and a capture zone between the first and second ends;
a fluid flow controller effective to variably impose a positive or negative pressure on the flow path to cause controlled fluid flow through the fluid flow path in a first or second direction at predetermined rates and effective to impose a pulse in said flow in said first or second direction sufficient to dislodge magnetic particles trapped in said capture zone;
a magnetic field source generating a fixed magnetic field, the source positioned in a fixed relationship to the fluid flow path whereby the field intercepts the fluid flow path in the capture zone; and
a detector positioned to detect a physical or chemical property of a fluid in the flow path.

43. (Original) The apparatus in accordance with claim 42 wherein the detector is an optical detector.

44. (Original) The apparatus in accordance with claim 42 wherein the fixed magnetic field source comprises a permanent magnet.

45. (Original) The apparatus in accordance with claim 42 wherein the fixed magnetic field source comprises an electromagnet.

46. (Original) The apparatus in accordance with claim 42 wherein the magnetic field has a field strength of from about 0.1 to about 2 kGauss/cm.

47. (Currently amended) The apparatus in accordance with claim 42 wherein the flow path in the capture/~~dispersion region~~ zone has a volume of from about 1 to about 50 uL.

48. (Original) The apparatus in accordance with claim 42 wherein the flow path has an average diameter of from about 0.1 to about 5 mm.

49. (Original) The apparatus in accordance with claim 42 wherein the fluid flow controller is effective to provide flow rates in the fluid flow path of up to about 2500 mm/s in either direction.

50. (Original) The apparatus in accordance with claim 42 wherein the controller includes a reversible pump in fluid communication with the fluid flow path.

51. (Currently amended) The apparatus in accordance with claim 42 wherein the fluid flow controller comprises:

a multiport selection valve including a primary port and a plurality of secondary ports, wherein a first secondary port is fluidly connected to the inlet of the fluid flow path;

a holding coil having a proximal end and a distal end; wherein the distal end is fluidly connected to the ~~main~~ primary port of the selection valve;

a three-way valve having a first port fluidly connected to the proximal end of the holding coil; a second port fluidly connected to a variable speed reversible pump; and a third port fluidly connected to a source of a wash composition.

52. (Currently amended) The apparatus in accordance with claim 42 51 wherein the variable speed reversible pump is a stepper-motor-driven syringe pump.

53. (Currently amended) The apparatus in accordance with claim 42 51 wherein the multiport selection valve, the three-way valve and the pump are controlled by a pre-programmed computer.

54. (Original) The apparatus in accordance with claim 42 wherein the flow path in the capture zone is substantially free from fixed magnetizable solid matrix structures.

55. (Currently amended) An apparatus, comprising:
a fluid flow path, the fluid flow path having first and second ends and a plurality of capture zones between the first and second ends;
a fluid flow controller effective to variably impose a positive or negative pressure on the flow path to cause controlled fluid flow through the fluid flow path in a first or second direction at predetermined rates and effective to impose a pulse in said flow in said first or second direction sufficient to dislodge magnetic particles trapped in at least one of said capture zone; and
a plurality of magnetic field sources, each source generating a fixed magnetic field, and each the source positioned in a fixed relationship to the fluid flow path whereby each field intercepts the fluid flow path in a capture zone;
wherein each capture zone is separated from one or more other capture zones by a zone that is substantially free from a magnetic field.

56. (Currently amended) An apparatus, comprising:
a fluid flow path means having first and second ends and a capture zone between the first and second ends;
means for providing in the fluid flow path a first mixture including a plurality of solid magnetic particles dispersed in a carrier medium;
means for variably imposing a positive or negative pressure on the fluid flow path means to cause controlled fluid flow through the fluid flow path in a first or second direction at predetermined rates;
a means for imposing a pulse in said flow in said first or second direction sufficient to dislodge magnetic particles trapped in said capture zone; and
means for providing a fixed magnetic field that intercepts the fluid flow path means in the capture zone.

57. (withdrawn) A method comprising:

passing a mixture including a plurality of solid magnetic particles dispersed in a carrier medium through a conduit extending through a fixed magnetic field at a first predetermined capture rate whereby magnetic particles become trapped in the field and thereby separated from the carrier medium to form a magnetic particle isolate;

passing a dispersion medium into the conduit and into contact with the magnetic particle isolate; and

pulsing the dispersion medium through the conduit at a first predetermined dispersion rate effective to move the magnetic particles from the magnetic field and suspend the magnetic particles in the dispersion medium.

58. (withdrawn) A method comprising:

passing a first mixture including a plurality of solid magnetic particles dispersed in a carrier medium through a conduit extending through a magnetic field at a first predetermined capture rate whereby magnetic particles become trapped in the field and thereby separated from the carrier medium to form a magnetic particle isolate;

releasing the magnetic particle isolate from the magnetic field by pulsing a dispersion medium through the conduit at a first predetermined dispersion rate effective to move the magnetic particles from the magnetic field and suspend the magnetic particles in the dispersion medium to provide a second mixture; and

recapturing the magnetic particles by passing the second mixture through the magnetic field in a direction opposite said passing of the first mixture, at a second predetermined capture rate whereby magnetic particles become trapped in the field and thereby separated from the carrier medium to form a magnetic particle isolate.

59. (withdrawn) The method in accordance with claim 58 wherein the first mixture has a different composition than the second mixture.